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# What Problems Are Prevalent Among Survivors of Critical Illness and Which of Those Are Consequences of Critical Illness?

Theodore J. Iwashyna

This topic covers an area of rapidly evolving research. As such, an exhaustive approach is guaranteed to be outdated by publication. Therefore this chapter seeks to provide an approach to the problems faced by survivors of critical illness with a focus on patients surviving acute respiratory distress syndrome (ARDS) and severe sepsis.

## WHAT PROBLEMS ARE PREVALENT AMONG SURVIVORS OF CRITICAL ILLNESS?

Survivors of critical illness must deal with many problems. Indeed, compared with an age-matched population, survivors of critical illness face nearly every medical complication imaginable. As is discussed in the next section, some of these problems reflect preexisting illnesses. In some cases, an exacerbation or complication of the preexisting condition led to the development of critical illness. However, regardless of when they developed, these long-term problems prevalent among critical illness survivors are real problems that survivors, their families, and their physicians need to face.

Some survivors of critical illness face a substantially elevated mortality after discharge from the hospital, a problem best documented for severe sepsis. For example, Quartin et al.<sup>1</sup> compared patients with severe sepsis in the 1980s to matched nonseptic patients hospitalized during the same time period. Among patients who had lived at least 180 days after their illness, patients with severe sepsis were 3.4 times more likely than controls (95% confidence interval: 2.3, 4.2) to die in the subsequent 6 months (i.e., days 181 to 365 after hospitalization). Indeed, among those who lived at least 2 full years, survivors of severe sepsis were still 2.2 times as likely as controls to die by year 5. Yende et al.<sup>2</sup> and Prescott et al.<sup>3</sup> have shown similar rates of excess postdischarge mortality among survivors of severe sepsis. In contrast, Wunsch et al.<sup>4</sup> looked at intensive care unit (ICU) patients with and without mechanical ventilation and compared them with the general population and with hospitalized controls; these authors suggested that there is substantial excess mortality

among patients who had undergone mechanical ventilation relative to the other groups, but that excess mortality occurred largely in the first 6 months postdischarge.

The term *post-intensive care syndrome* (PICS) was coined to provide an intellectual framework for organizing the problems prevalent among those who survive this excess mortality.<sup>5,6</sup> A working description of PICS was developed over several years and involved extensive contributions from stakeholders—including patients, families, caregivers, administrators, and others—within critical care and throughout the broader medical and rehabilitation communities. Within PICS, it is valuable to consider three broad domains: physical health, cognitive impairment, and mental health.

Most work after critical illness has focused on the presence and persistence of neuromuscular weakness. In my opinion, enduring weakness, which can be profound and disabling, is the central patient-centered physical problem facing the population of survivors as a whole. Abnormalities of motor function, united under the useful umbrella of “ICU-acquired weakness,” include myopathies and polyneuropathies.<sup>7</sup> The biology of this syndrome remains an active area of research, but there is little evidence that the origin (nerve or muscle) of the underlying defect affects either prognosis or specific treatment. Physical and occupational therapies are the mainstay of recovery.<sup>8</sup>

Other physical problems are common but less studied. Transient and enduring renal failure have been noted.<sup>9</sup> High rates of cardiovascular disease are reported.<sup>10</sup> Dyspnea and low exercise tolerance, even in the face of seemingly normal or near normal pulmonary function tests, are ubiquitous after severe ARDS.<sup>11,12</sup> Other survivors report subglottic stenosis and profound cosmetic changes.<sup>10</sup> High rates of cachexia, injurious falls, incontinence, and impaired hearing and vision have all been reported.<sup>13</sup>

A spectrum of cognitive impairment is also common after critical illness. Abnormalities range from dysfunction in specific tasks (defects in executive function are particularly common) to frank cognitive impairment. The prevalence seems to be high, although there is disagreement regarding how severe an abnormality must be to be “bad

enough to be counted.<sup>14-19</sup> Patients who experience severe delirium in the ICU may be at greater risk to lose cognitive function at a later time,<sup>20</sup> but the duration of the cognitive dysfunction is probably months to years; therefore it is unlikely to be a simple extension of ICU- or hospital-acquired delirium.

There is also evidence that ICU survivors experience high degrees of depression, anxiety, and posttraumatic stress disorder (PTSD). Assessments of depression with the Hospital Anxiety and Depression Scale (HADS) have tended to emphasize the PTSD finding.<sup>21-23</sup> In contrast, more recent work by Jackson and colleagues<sup>24</sup> suggested that the HADS may be insufficiently sensitive to somatic symptoms of depression and that symptoms attributed to PTSD were not in fact tied to the critical illness experience. Although these issues are being addressed, it is clear that many patients have significant emotional disorders.<sup>25,26</sup>

In summary, survivors of critical illness face a wide array of problems. Only some of these have been adequately studied, and there are specific interventions for even fewer. These problems lead to high rates of ongoing health-care resource use and frequent rehospitalization.<sup>3,27,28</sup> There is growing recognition that the consequences of critical illness also place substantial strain on families of ICU survivors, who often bear the brunt of high levels of ongoing informal care.<sup>29-37</sup>

In the face of such high prevalence, it is understandable that critical care practitioners may develop a certain nihilism or sense of hopelessness. Obviously, this is an issue that must be addressed by each involved individual. However, it seems important to stress that the inability to save everyone does not mean that many are not fully saved. The newly appreciated prevalence of PICS represents a problem to be tackled and eventually solved, not an inevitable fate to which all ICU patients are doomed. Indeed, as Cuthbertson and colleagues noted in their longitudinal cohort of Scottish sepsis survivors, "At five years all patients stated they would be willing to be treated in an ICU again if they become critically ill... [and] 80% were either very happy or mostly happy with their current QOL [quality of life]."<sup>38</sup>

## WHICH OF THE PROBLEMS FACED BY SURVIVORS ARE CONSEQUENCES OF CRITICAL ILLNESS?

It is sometimes rhetorically useful to frame studies of long-term consequences as extremes on a spectrum: preexisting problem or conditions caused entirely by critical illness. One unfortunate consequence of such a dichotomy is the development of a false sense of hierarchy—asking, "which is more important?" It is rather much more valuable to examine the extent to which acute changes and preexisting conditions contribute in any given patient.

Perhaps the best research on this particular problem lies in the domain of cognitive impairment after critical illness. A large group of investigators followed 5888 older Americans in the Cardiovascular Health Study, a population-based observational cohort.<sup>19</sup> Patients were examined every year with the Teng Modified Mini-Mental Status examination. Shah et al.<sup>19</sup> noted that patients who went on to have pneumonia were more likely to have lower premorbid

cognitive scores and scores that had been declining more rapidly before the development of pneumonia. However, whatever their baseline trajectory, patients who contracted pneumonia had an increasingly rapid transition to dementia. Iwashyna et al.<sup>18</sup> found similar results with severe sepsis, and Ehlenbach et al.<sup>39</sup> noted this finding in a group of severely critical ill patients.

In other cases, findings have been less consistent. Wunsch et al.<sup>25</sup> used elegantly detailed Danish records to show that depression and other mental health disorders were diagnosed much more commonly in patients after critical illness with mechanical ventilation than in the years before the critical illness. However, Davydow et al.<sup>26</sup> showed that U.S. survivors of severe sepsis did not exhibit a change in the (already very high) level of depressive symptoms present before or after severe sepsis. It is possible to reconcile such findings by attributing them to the known low sensitivity of general medical practice for the detection of depression and an increased level of surveillance in the years after critical illness. The Davydow findings might also be explained by an insufficiently responsive scale for symptoms; however, the data are not yet conclusive.

In some cases—often with too few studies for there to be much conflict—it appears that the prevalent problems after critical illness are primarily the result of preexisting morbidity. Further complicating such work is the fact that older Americans are at increasing risk for both critical illness and potential complications. Thus, work in the Health and Retirement Study showed dramatic increases in rates of injurious falls and incontinence in survivors of severe sepsis relative to both the general population of older adults and even compared with the same patients when measured presepsis.<sup>13</sup> However, any apparent effect of sepsis disappeared when the "morbidity growth curve" of older Americans was controlled (i.e., their presepsis trajectory of increasing development of morbidity).

In summary, patients who have critical illness typically had both worse level of functioning than the general population before the development of their critical illness and were on trajectories of more rapid decline before their critical illness. However, it is common to have even worse function after critical illness. This finding is not universal; for example, no such exacerbations after critical illness were detectable for geriatric conditions such as injurious falls. It may also not be true for impaired quality of life, particularly because people may be able to adapt to their new postcritical illness deficits.

## WHY DOES IT MATTER WHETHER THE PROBLEM PRECEDES CRITICAL ILLNESS OR IS A CONSEQUENCE OF CRITICAL ILLNESS?

Having established that there are substantial problems that are highly prevalent among survivors of critical illness, it is increasingly time to ask what can be done to make things better. The next section discusses specific strategies. However, there are generally three strategies that can be informed by this approach: (1) in-ICU prevention, (2) treatment and remediation, and (3) triage. In-ICU

prevention strategies are only effective for problems that develop over the course of critical illness; although one can prevent it from becoming worse, one cannot prevent a problem that already exists. Therefore it is important to know which conditions present in each individual patient, as opposed to the population of survivors as a whole, did or did not preexist the development of critical illness.

"When newly acquired diagnoses are evaluated, it is essential to distinguish the degree of morbidity consequent of critical illness from complications arising from interventions to treat the disorder and support the patient. For example, ICU-acquired weakness is common in ICU survivors. However, it is difficult to determine to what extent this disability results from the critical illness itself as opposed to the treatment modalities, including prolonged bed rest; use of neuromuscular blocking agents, antibiotics, or other drugs; decreased respiratory muscle activity resulting from mechanical ventilation; and inadequate metabolic/nutritional support. Indeed, PICS is an acronym for "post-intensive care syndrome," not "postcritical illness syndrome," but health-care providers should not let this bold (but untested), implicit assertion provide false assurances as to where the problems may lie. Misattribution to management of problems that are really a consequence of critical illness itself could lead to faulty triage decisions, in which patients with a critical illness are kept out of the ICU to spare them the perceived risk of exposure to ICU-induced consequences. However, such triage would also preclude such patients from receiving ICU-possible improvements in care. However, to the extent that ICU care is of lower marginal value and prone to excess interventions, invasive monitoring, and bed rest, then such a decision would be fully appropriate. Conversely, an incorrect belief that a complication is a component of the underlying disorder may lead to overuse of therapy; for example, it appears that less sedation reduces the psychological sequelae of critical care rather than providing the preventive amnesia that some once hoped it would. There is an urgent need for objective data to inform this debate; in particular, data should not merely catalog the problems in one place but also catalog comparative effectiveness research of care in alternative settings.

### **GIVEN THE ABSENCE OF PROVEN SPECIFIC THERAPIES, WHAT IS A PRAGMATIC APPROACH TO IMPROVING LONG-TERM CONSEQUENCES FACED BY PATIENTS SURVIVING CRITICAL ILLNESS?**

Patients surviving critical illness labor under a complex burden of problems—some newly developed as a consequence of the acute episode, some present before critical illness but exacerbated by the episode to the point of decompensation, and some preexisting in occult form that are unmasked critical illness. There are no proven therapies specifically remediating long-term problems after the ICU. There are several potentially promising approaches or interventions that could be initiated in the ICU. A pragmatic approach, which is based on the work of Margie Lachman in a different setting,<sup>40</sup> that the author

has found to be clinically valuable involves six steps detailed here:

1. *Prevention:* There is frustratingly little to prove that excellent in-ICU care prevents post-ICU problems. However, the physiologic rationale that minimizing the extent of critical illness is an essential step to improving the lives of patients who survive the ICU is highly compelling. It is my practice to emphasize aggressive sepsis detection and resuscitation, low tidal volume ventilation, sedation minimization, and early mobilization of mechanically ventilated patients.
2. *Protection:* That ICU patients frequently experience discontinuities of care after transfer out of the ICU is well documented.<sup>41</sup> Essential home medications are never restarted. Antipsychotics intended only for short-term delirium management are continued for prolonged periods.<sup>42,43</sup> The receiving team is not made aware of the appearance of new radiographic findings, and follow-up does not occur.<sup>44</sup> There are multiple process-of-care efforts to prevent such discontinuities that would seem to be essential. Furthermore, there may be roles for early mobility, sedation minimization, patient diaries, and other yet unproven therapies that will prevent ICU patients from having new neuromuscular and emotional deficits in the first place.
3. *Treatment:* Previously unrecognized or undiagnosed problems often are uncovered in the ICU. In some cases (e.g., the patient whose diabetes first presents as diabetic ketoacidosis), there are well-established procedures not only to correct the acute problem but also to ensure appropriate follow-up, including education and communication with primary care providers. However, other conditions, in particular depression and mental health issues, are often neglected. A balanced approach to improving life after the ICU must ensure appropriate follow-up for all new problems diagnosed or likely to be exacerbated in the ICU. Good approaches to specifically ensure appropriate follow-up after the ICU are lacking, but work on transitions of care for geriatric patients may provide promising models.
4. *Remediation:* The evidence increasingly suggests that disability after critical illness is rooted in muscle weakness, cognitive impairment, and lack of social support. Many practitioners strongly recommend early and ongoing physiotherapy for all patients in the ICU, with follow-up as an outpatient when appropriate. However, the appropriate approach to physiotherapy should be one of preventing any loss of functioning while in the ICU as opposed to only treating those with demonstrable weakness. Moreover, work by Hopkins and others<sup>45</sup> has shown that physical therapy in the ICU may also have important cognitive and psychiatric benefits. Also, it is essential that a patient's family or other support group be intimately involved in the process of providing ICU care. Netzer<sup>36</sup> has defined a "family ICU syndrome." His work and others' show the incredible toll that ICUs take on families. However, if patients are critically vulnerable in the period immediately after discharge, family participation may be an essential and underused determinant of whether the patients have a trajectory of recovery or a trajectory of disability.



5. *Compensation*: Even with the best medical care and physical therapy, some patients will have new problems after the ICU. There is an ongoing struggle to find a systematic approach to evaluating their needs. The model of a Comprehensive Geriatrics Assessment may hold great promise, but it needs to be customized to the ICU.<sup>46</sup> In this approach, there is a structured questionnaire tied to initial interventions to assess a range of potential needs. The sort of pragmatic assistance that geriatricians routinely provide to allow weak older patients to stay in their home may be of great value to ICU patients in their recovery.
6. *Enhancement*: The next frontier of recovery of critical illness will be finding ways to empower survivors to help each other by developing innovative peer support models. This approach allows patients to become partners in discovering new approaches to facilitate recovery. Such groups have fundamentally transformed recovery from cancer, stroke, Alzheimer disease, and other disabling conditions. This powerful tool holds enormous promise for improving outcomes after the ICU.

## CONCLUSION

Many, but not all, patients have a range of physical, cognitive, and emotional challenges after critical illness. There are a limited number of validated tools to identify patients at risk for PICS.<sup>14</sup> Likewise, critical care professionals have yet to develop specific, validated therapies to prevent or treat these multifactorial problems. However, there is reason to believe that emerging techniques in patient management and rehabilitation offer the hope of improving the lives of survivors.

### AUTHOR'S RECOMMENDATIONS

- A significant proportion of patients have range of physical, cognitive, and emotional challenges after critical illness; this is known as PICS (post-intensive care syndrome).
- There is growing recognition that the consequences of critical illness also places substantial strain on families of ICU survivors, who often bear the brunt of high levels of ongoing informal care.
- Patients who have critical illness typically had both worse functionality than the general population and were on trajectories of more rapid decline before their critical illness.
- There are a limited number of validated tools to identify patients at risk for PICS. Three strategies that can be used to prevent PICS are (1) in-ICU prevention, (2) treatment and remediation, and (3) triage.
- Clinicians have yet to develop specific, validated therapies to prevent or treat these multifactorial problems.
- There is reason to believe that emerging techniques in patient management and rehabilitation offer the hope of improving the lives of survivors.

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